What is Claimed Is:

1. A small interfering RNA comprising 15-25 nucleotides complementary to a target nucleic acid sequence, wherein the RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

2. The small interfering RNA according to Claim 1, wherein all of the internucleoside linkages are chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

3. The small interfering RNA according to Claim 1, wherein said small interfering RNA is in a form chosen from the single-stranded form comprising the antisense strand, and the double-stranded form comprising both sense and antisense strands.

4. The small interfering RNA according to Claim 1, wherein the RNA further comprises at least one covalently conjugated lipid moiety.

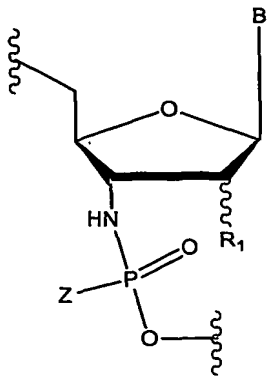
5. The small interfering RNA according to Claim 4, wherein at least one covalently conjugated lipid moiety is covalently conjugated to the antisense strand; or wherein one lipid moiety is covalently conjugated to the 5' or 3' terminus of the RNA, and the lipid moiety is chosen from fatty acids, sterols, and hydrocarbons.

6. A compound comprising the structure:

$$O\text{-}(x\text{-}L)_n$$

wherein

- O is a riboamidate of formula:



wherein R_1 is chosen from fluorine and OR_2, R_2 is chosen from hydrogen and lower alkyl , B is chosen from purines, pyrimidines, and analogs thereof, and Z is chosen from oxygen and sulfur, and further wherein the riboamidate comprises a sequence of 15 to 25 bases, and said sequence is at least partially complementary to a selected target sequence;

- L is a lipid moiety;

- x is an optional linker; and

- n is an integer ranging from 1 to 5, wherein if n>1, each additional (x-L) component may be, independently, the same or different.

7. The compound according to Claim 6, wherein O is a riboamidate comprising a sequence of 19 to 23 bases complementary to a selected target sequence; or wherein Z is oxygen; or wherein Z is sulfur; or wherein L is a lipid chosen from substituted and unsubstituted fatty acids and sterols; or wherein L is chosen from substituted and unsubstituted hydrocarbons; or wherein n = 1 and the (x-L) component is covalently conjugated to the 5'

terminus of the riboamidate O; or wherein n = 1 and the (x-L) component is covalently conjugated to the 3' terminus of the riboamidate O; or wherein n = 2, one (x-L) component is covalently conjugated to the 5' terminus and one independently chosen (x-L) component is covalently conjugated to the 3' terminus; or wherein n = 1 and the (x-L) component is covalently conjugated to a nucleobase on the riboamidate O; or wherein the riboamidate comprises nucleobases, and 100% of the nucleobases in the riboamidate are ribonucleobases; or wherein the riboamidate comprises a sequence of 15 to 25 bases that is exactly complementary to a selected target sequence.

8. The compound according to Claim 7, wherein L is chosen from fatty acids substituted with at least one fluorine; or wherein L is chosen from hydrocarbons substituted with at least one fluorine; or wherein at least 80% of the nucleobases in the riboamidate are ribonucleobases; or wherein at least 60% of the nucleobases in the riboamidate are ribonucleobases.

9. An antisense strand of a small interfering RNA, comprising a compound according to Claim 6.

10. A composition comprising at least one small interfering RNA according to Claim 1 in an amount effective to modulate the expression of at least one gene; or at least one compound according to Claim 6 in an amount effective to modulate the expression of at least one gene.

11. A method for treating a mammal, comprising administering to the mammal at least one small interfering RNA according to Claim 1; or comprising administering to the mammal at least one compound according to Claim 6.

12. A method for effecting the post-transcriptional silencing of at least one gene, comprising administering to a mammal in need of such post-transcriptional silencing at least one a small interfering RNA comprising 15-25 nucleotides complementary to a target nucleic acid sequence, wherein the RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

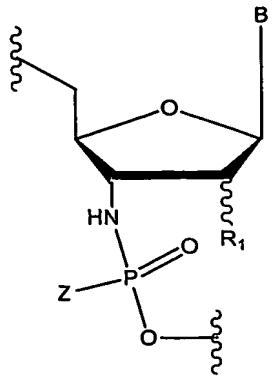
13. The method according to Claim 12, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety; or wherein the at least one gene encodes at least one mRNA chosen from cellular mRNAs and viral mRNAs; or wherein the at least one gene is an oncogene; or wherein the at least one gene is a viral gene.

14. A method for effecting the post-transcriptional silencing of at least one gene, comprising administering to a mammal in need of such post-transcriptional silencing at least one compound comprising the structure:

$$O\text{-}(x\text{-}L)_n$$

wherein

- O is a riboamidate of formula:



wherein R_1 is chosen from fluorine and OR_2, R_2 is chosen from hydrogen and lower alkyl , B is chosen from purines, pyrimidines, and analogs thereof, and Z is chosen from oxygen and sulfur, and further wherein the riboamidate comprises a sequence of 15 to 25 bases, and said sequence is at least partially complementary to a selected target sequence;

- L is a lipid moiety;

- x is an optional linker; and

- n is an integer ranging from 1 to 5, wherein if n>1, each additional (x-L) component may be, independently, the same or different.

15. The method according to claim 14, wherein the at least one gene encodes at least one mRNA chosen from cellular mRNAs and viral mRNAs; or wherein the at least one gene is an oncogene; or wherein the at least one gene is a viral gene.

16. A method for regulating the expression of genes in an organism, comprising administering to a mammal in need of such regulation at least one small interfering RNA comprising 15-25 nucleotides complementary to a target nucleic acid sequence, wherein the RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

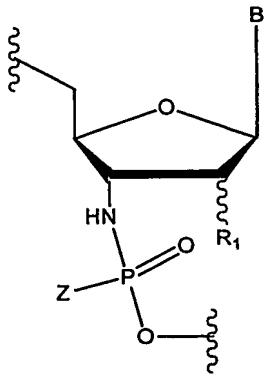
17. The method according to Claim 16, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

18. A method for regulating the expression genes in an organism, comprising administering to said organism at least one compound comprising the structure:

$$O\text{-}(x\text{-}L)_n$$

wherein

- O is a riboamidate of formula:



wherein R_1 is chosen from fluorine and OR_2, R_2 is chosen from hydrogen and lower alkyl , B is chosen from purines, pyrimidines, and analogs thereof, and Z is chosen from oxygen and sulfur, and further wherein the riboamidate comprises a sequence of 15 to 25 bases, and said sequence is at least partially complementary to a selected target sequence;

- L is a lipid moiety;

- x is an optional linker; and

- n is an integer ranging from 1 to 5, wherein if n>1, each additional (x-L) component may be, independently, the same or different.

19. A single-stranded small interfering RNA that inhibits the expression of an endogenous mammalian target RNA sequence, wherein the single-stranded small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

20. The single-stranded small interfering RNA according to Claim 19, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety; or wherein the target RNA sequence is encoded by a human gene.

21. A double-stranded small interfering RNA that inhibits the expression of an endogenous mammalian target RNA sequence, wherein the double-stranded small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

22. The double-stranded small interfering RNA according to Claim 21, wherein the target RNA sequence is encoded by a human gene; or wherein the RNA further comprises at least one covalently conjugated lipid moiety.

23. A small interfering RNA that modulates expression of a human immunodeficiency virus (HIV) gene,

wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

24. The small interfering RNA according to Claim 23, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

25. A small interfering RNA that modulates expression of a beta site APP-cleaving enzyme (BACE) gene,

wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

26. The small interfering RNA according to Claim 25, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

27. A small interfering RNA that modulates expression of an EGFR gene, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

28. The small interfering RNA according to Claim 27, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

29. A small interfering RNA that modulates expression of a nucleic acid molecule encoding K-Ras, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

30. The small interfering RNA according to Claim 29, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

31. A small interfering RNA that modulates expression of a prostaglandin D2 receptor (PTGDR) gene, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

32. The small interfering RNA according to Claim 31, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

33. A small interfering RNA that modulates expression of an epidermal growth factor receptor (EGFR) gene, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

34. The small interfering RNA according to Claim 33, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

35. A small interfering RNA that modulates expression of a prostaglandin D2 receptor PTGDR gene, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

36. A small interfering RNA according to Claim 35, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

37. A small interfering RNA that modulates expression of an ADORA1 gene, wherein the small interfering RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

38. The small interfering RNA according to Claim 37, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

39. The use of a small interfering RNA to modulate the expression of an endogenous mammalian target gene, wherein said RNA comprises at least one internucleoside linkage chosen from ribo-N3'→ P5' phosphoramidate (NP) and ribo-N3'→ P5' thiophosphoramidate (NPS) linkages.

40. The use according to Claim 39, wherein the small interfering RNA further comprises at least one covalently conjugated lipid moiety.

41. A medicament comprising the small interfering RNA of Claim 1 or Claim 6.

42. The use of a small interfering RNA according to Claim 1 or Claim 6 for preparing a medicament.

43. The use of a single-stranded small interfering RNA according to Claim 19 for preparing a medicament.

44. The use of a double-stranded small interfering RNA according to Claim 21 for preparing a medicament.

45. The use of a small interfering RNA according to any of Claim 23 for preparing a medicament